REMARKS/ARGUMENTS

By the foregoing amendment, the specification has been amended to correct the year of the Murdock reference on page 3 and to insert sequence ID numbers, were appropriate, on page 10. Also, claim 1 has been amended to further clarify the invention and dependent claim 5 has been cancelled in view of the amended language of claim 1. Additionally, typographical errors have been corrected in claims 2-4. No new matter has been added. Reconsideration is respectfully requested.

The foregoing amendments have remedied all technical objections to the claims and specification stated in the Office Action.

In the Office Action, the *only* rejection of dependent claim 5 was for lack of enablement under 35 U.S.C. §112, first paragraph. The Office Action contains no Section 102/103 or written description rejections of dependent claim 5.

By the present amendment, Applicant has amended the limitation of dependent claim 5 into independent claim 1 and claim 5 has been cancelled. As amended, independent claim 1 recites a method for diagnosis of a disorder associated with the development of beta amyloid deposits or fibrils in a human or animal subject or assessing the efficacy of treatment rendered to the subject for such disorder, said method comprising the steps of:

> A) determining the presence of mtDNA CR mutations; and
>
> B) comparing a mtDNA CR value obtained by the quantitative determination made in Step A with a mtDNA CR value representative of subjects who suffer from a disorder associated with the development of beta amyloid deposits or fibrils.

At page 7 (numbered paragraph 9) of the Office Action, the Examiner concedes that the application is enabling for "determining the presence of mtDNA CR mutations." Thus, there is no issue regarding enablement of Step A of claim 1. The only remaining issue is whether this application contains disclosure which adequately enables Step B of amended claim 1. For the reasons articulated below, when the applicable principles of law are correctly applied, it must be

concluded that amended claim 1 (including its Step B) is fully enabled by the originally filed disclosure.

In general, the present application as a whole, enables a person of ordinary skill in the art to generate *reference data* by measuring mtDNA CR mutations in groups of patients known to have pathological beta amyloid deposits or fibrils as well as a group of normal individuals who do not suffer from such disorders. The present application (as well as established statistical methodology) further enables one of skill in the art to compare mtDNA CR mutations measured in a test subject with the reference data to determine whether or not the test subject also has pathological beta amyloid deposits or fibrils. The task of generating mtDNA CR reference data for normal controls and diseased patients and then comparing those reference data to test subject data clearly does not constitute "undue experimentation."

Also, in Example 1 of the present application, frontal cortex tissue samples were taken from the brains of 63 cadavers that were pathologically confirmed as either having Alzheimer's disease (AD; 23 out of 63) or not having AD (normal, control; 40 out of 63). The mtDNA hypervariable region (np-16000-100) of these samples were then sequenced, controlling for polymorphic differences common for intercontinental comparisons and spurious amplification of nuclear DNA (nDNA)-encoded, mtDNA pseudogenes, when a mutation in the T414 gene was clearly detected in the Alzheimer's disease samples, as seen Figs 2C and 2E. In addition, in Fig. 1B, the number of heteroplasmic mutations in mtDNA CR regulatory elements in AD and control (non AD) brains have been tabulated. In this Example, Applicants have unequivocally established a link between mutations such as, for example, in T414G, in mtDNA CR and presence of Alzheimer's disease because the T414G mutation was clearly detected only in Alzheimer's disease samples. Notably, Alzheimer's disease is a disorder associated with the development of beta amyloid deposits or fibrils. In addition, by the Examiner's own assertion, Applicants have also laid out and enabled a person of ordinary skilled in the art with the method for determining the presence of and quantity of mtDNA CR mutations (see for example, Fig. 1B). Thus, taken together, these portions of the application do enable a person of ordinary skill in the art to practice the diagnostic method of Claim 1 without any or undue experimentation.

Accordingly, all claims as presently amended are believed to be fully enabled and withdrawal of the lack of enablement rejection is respectfully requested.

Conclusion

For the foregoing reasons, the application is believed to be in condition for allowance and issuance of a notice of allowance is earnestly solicited. A three (3) month extension is hereby petitioned for under 35 U.S.C. 1.136 and the fee for such extension will be paid electronically concurrently with filing of this response. The Commissioner is hereby authorized to charge any underpayment, or to credit any overpayment, to Deposit Account No. 50-0878.

Date: February 22, 2011

Respectfully submitted,
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